

WHAT IS CLAIMED IS:

1 1. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:

3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 comprising a protein, a polypeptide, a peptide, a nucleic acid, a polynucleotide, an
7 mRNA, a small organic molecule, a lipid, a fat, a glycoprotein, a glycopeptide, a
8 carbohydrate, an oligosaccharide, a chromosomal abnormality, a whole cell having a
9 marker molecule, a particle, a secreted molecule, an intracellular molecule, and a complex
10 of a plurality of molecules.

1 2. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:

3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 comprising RNA, DNA, protein, polypeptide, or peptide form of a marker selected from
7 the group consisting of a receptor, a ligand, a protein factor, an antigen, an antibody, an
8 enzyme, a soluble protein, a cytosolic protein, a cytoplasmic protein, a tumor suppressor,
9 a cell surface antigen, a phospholipid, a lipoprotein, a hormone responsive protein, a
10 differentiation associated antigen, a proliferation associated antigen, a metastasis
11 associated antigen, an integral membrane protein, a protein that participates in an
12 apoptosis pathway, a protein that participates in a transcriptional activation pathway, a
13 cell adhesion molecule, an extracellular matrix protein, a proteolipid, a cytokine, a
14 basement membrane protein, a mucin-type glycoprotein, a histone, a ribonucleoprotein, a
15 sialic acid, a bone matrix protein, a carbohydrate antigen, a nuclear protein, a nuclear
16 phosphoprotein, a proto-oncogene, an oncogene, an apolipoprotein, a serine protease, a
17 tumor rejection antigen, a surfactant protein, a cell death protein, a zinc endoprotease, and
18 a trefoil gene.

1 3. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:

3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 comprising RNA, DNA, protein, polypeptide, or peptide form of a marker selected from
7 the group consisting of a chemokine, a lectin, an integrin, a selectin, a keratin, an
8 interleukin, a taxin, a ferritin, a lipocalin, a laminin, a cyclin, a relaxin, a nuclein, a
9 caspase, a melanoma-associated antigen, a macrophage inflammatory protein, a gap
10 junction protein, a calcium binding protein, an actin binding protein, a phospholipid
11 binding protein, a heat shock protein, a cell cycle protein, an activator of tyrosine and
12 tryptophan hydroxylase, a member of the tumor necrosis factor family of proteins, a
13 member of the transforming growth factor alpha family of proteins, a member of the
14 transforming growth factor beta family of proteins, a member of the Bcl2 family of
15 proteins, a Bcl2-interacting protein, a Bcl2-associated protein, a member of the
16 vasopressin/oxytocin family of proteins, and a member of the CCAAT/enhancer binding
17 protein family of proteins.

1 4. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:

3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 wherein the marker is an enzyme and the enzyme comprises an RNA, DNA, protein,
7 polypeptide, or peptide form of an enzyme selected from the group consisting of a
8 phosphorylase, a phosphatase, a decarboxylase, an isoenzyme, a kinase, a protease, a
9 nuclease, a peptidase, a protease, a DNase, an RNase, an aminopeptidase, a
10 topoisomerase, a phosphodiesterase, an aromatase, a cyclooxygenase, a hydroxylase, a
11 dehydrogenase, a metalloproteinase, a telomerase, a reductase, a synthase, an elastase, a
12 tyrosinase, a transferase, and a cyclase.

1 5. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:
3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 wherein the marker is a receptor and the receptor comprises an RNA, DNA, protein,
7 polypeptide, or peptide form of a receptor selected from the group consisting of
8 a steroid hormone receptor, a growth factor receptor, a kinase receptor, a
9 G-protein linked receptor, a TNF family receptor, a tyrosine kinase receptor, a
10 vasopressin receptor, an oxytocin receptor, and a serine protease receptor.

1 6. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:
3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 wherein the marker is a protein factor and the factor comprises an RNA, DNA, protein,
7 polypeptide, or peptide form of a factor selected from the group consisting of a growth
8 factor, a proteolytic factor, a stromal cell factor, an epithelial cell factor, an angiogenesis
9 factor, an epithelial cell factor, an angiogenic factor, and a colony stimulating factor.

1 7. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:
3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 wherein the marker is an inhibitor and the inhibitor comprises an RNA, DNA, protein,
7 polypeptide, or peptide form of an inhibitor selected from the group consisting of an
8 inhibitor of a cyclin, an inhibitor of a cyclin complex, a serpin, an inhibitor of proteolytic
9 degradation, a tissue inhibitor of a metalloprotease, and an angiogenesis inhibitor.

1 8. A method of identifying a patient having breast cancer or breast
2 precancer, said method comprising:
3 providing a ductal fluid sample from one duct of a breast of a patient, said
4 fluid not mixed with ductal fluid from any other duct of the breast;
5 examining the ductal fluid sample to determine the presence of a marker
6 comprising a protein, a polypeptide, a peptide, a nucleic acid, a polynucleotide, an
7 mRNA, a small organic molecule, a lipid, a fat, a glycoprotein, a glycopeptide, a
8 carbohydrate, an oligosaccharide, a chromosomal abnormality, a whole cell having a
9 marker molecule, a particle, a secreted molecule, an intracellular molecule, and a complex
10 of a plurality of molecules;

11 wherein the marker is capable of differentiating between any two of
12 cytological categories consisting of normal, abnormal, hyperplasia, atypia, ductal
13 carcinoma, ductal carcinoma in situ (DCIS), ductal carcinoma in situ - low grade (DCIS-
14 LG), ductal carcinoma in situ - high grade (DCIS-HG), invasive carcinoma, atypical mild
15 changes, atypical marked changes, atypical ductal hyperplasia (ADH), insufficient
16 cellular material for diagnosis, and sufficient cellular material for diagnosis.

1 9. A method as in any of claims 1-7 further comprising analyzing the
2 ductal fluid for abnormal cytology.

1 10. A method as in any of claims 1-8 wherein the ductal fluid is
2 retrieved by placing a ductal access tool in the duct and infusing fluid into the duct
3 through the tool and retrieving from the accessed duct through the tool a portion of the
4 infused fluid mixed with ductal fluid.

1 11. A method as in any of claims 1 -8 wherein the method is repeated
2 for more than one duct on a breast.

1 12. A method as in any of claims 1-8 wherein the method is repeated
2 for a plurality of ducts on a breast.

1 13. A method for identifying a patient having breast cancer or breast
2 precancer, said method comprising:

3 providing a ductal fluid sample from at least one duct of a breast of the
4 patient; and

5 examining the ductal fluid sample to determine the presence of a marker
6 comprising an expression product of a gene encoding a nuclear matrix protein.

1 14. A method as in claim 13, wherein the expression product
2 comprises a nucleic acid or a polypeptide.

1 15. A method as in claim 13, wherein the expression product
2 comprises RNA.

1 16. A method as in claim 13, wherein the expression product
2 comprises a protein or a part of a protein.

1 17. A method as in claim 13, wherein the nuclear matrix protein is
2 selected from the group consisting of lamin A, lamin B, lamin C, a peripheral matrix
3 protein, nuclear mitotic spindle apparatus protein (NuMA), topoisomerase II, and an
4 internal nuclear matrix protein.

1 18. A method as in claim 13, wherein the expression product is a
2 polypeptide and examining comprises contacting the polypeptide marker with an antibody
3 that specifically binds a portion of the polypeptide.

1 19. A method as in claim 13, wherein the expression product is a
2 nucleic acid and examining comprises detecting the presence of the nucleic acid.

1 20. A method as in claim 19, wherein detecting the presence of the
2 nucleic acid comprises amplifying the nucleic acid.

1 21. A method as in claim 13, wherein providing the ductal fluid sample
2 comprises obtaining the sample from the breast.

1 22. A method as in claim 13, wherein providing the ductal fluid sample
2 comprises receiving a sample which had been previously obtained.

1 23. A method as in claim 13, wherein the fluid was obtained by nipple
2 aspiration of the milk ducts.

1 24. A method as in claim 13, wherein the fluid sample was obtained by
2 washing the ductal lumen and retrieving fluid and cells from the lumen.

1 25. A method as in claim 13, wherein the fluid collected is from a
2 single duct.

1 26. A method as in claim 13, wherein the fluid is collected from a
2 plurality of ducts.

1 27. A system for diagnosing breast cancer or precancer comprising a
2 tool to retrieve ductal fluid from a breast duct and instructions for use to determine the
3 presence of a marker identified in any of claims 1-8.

1 28. A system for diagnosing breast cancer or precancer comprising a
2 tool to retrieve ductal fluid from a breast duct and instructions for use to determine the
3 presence of a marker identified in any of claims 13-26.